REMARKS

Claims 51 and 53-58 were pending in the subject application. By this Amendment, applicants have amended claims 51 and 57, and added new claims 59 and 60. Support for amended claim 51 may be found *inter alia*, in the specification at page 2, line 17; page 4, lines 22-23; page 11, lines 31-34; page 12, lines 11-13; page 13, lines 10-22; page 22, lines 8-30; page 35, lines 32-34; page 36, lines 2-5. Applicants have amended claim 57 to delete the multiple dependency to claim 56 and have added new claims 59 and 60 which corresponds to this deleted subject matter of previously pending claim 57 and 58. Applicants maintain that no issue of new matter is raised by these amendments. Upon entry of this Amendment, claims 51 and 53-60 will be pending and under examination.

Rejection Under 35 U.S.C. §112, First Paragraph:

In the June 15, 2006 Final Office Action, the Examiner maintained the rejection of then pending claims 51 and 53-58 as allegedly failing to comply with the written description requirement. Specifically, the Examiner stated that applicants were not in possession of an antibody against CCR5 even though CCR5 was known to mediate HIV-1 entry, its sequence was in the public domain prior to the effective filing date of the subject application, and a person skilled in the art knew how to make antibodies.

Applicants understand that the Examiner has put forward two rationales in support of this rejection as follows:

1. On page 4 of the June 15, 2006 Final Office Action, the Examiner stated that the claims are not adequately described because the specification only discloses a functional characteristic of CCR5 antibodies, i.e. binding to CCR5, but does not disclose any specific sequences or partial structures of the antibodies, or physical and/or chemical properties of the antibodies against CCR5. In support of this assertion, the Examiner cited M.P.E.P.

§2163 and stated that "if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is 'not [a] sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

2. On page 5 of the June 15, 2006 Final Office Action, the Examiner stated that the specification fails to provide adequate written description for a genus of CCR5 antibodies. In support of this assertion, the Examiner cited *Regents of the University of California v. Eli Lilly & Co.*, [119 F.3d 1559,] 43 USPQ2d 1398 [(Fed. Cir. 1997)], wherein the court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Citing *In Re Wilder*, 736 F.2d 1516, 222 USPQ2d 369 [(Fed. Cir. 1984)], the Examiner further stated that the written description requirement "requires a description not an indication of a result that one might achieve if one made the invention."

Response to Examiner's Rationale #1

In response to the Examiner's rationale 1, applicants respectfully traverse the Examiner's ground of rejection and maintain that claim 51 as amended herein and claims 53-60 dependent thereon satisfy the written description requirement of 35 U.S.C. §112, first paragraph.

Applicants' invention as recited in amended claim 51 provides an isolated antibody which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell, wherein the antibody inhibits fusion of HIV-1 or a HIV-1 infected cell to the CD4+ cell, so as to thereby inhibit HIV-1 infection of such CD4+ cell.

Applicants first note that, as indicated in M.P.E.P. §2163.04, a description as filed is presumed to be adequate and the examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in applicants' disclosure a description of the invention defined by the claims to rebut the presumption that the description is adequate, citing *In Re Wertheim*, 541 F.2d 257, 262, 1991 USPQ 90, 96 (CCPA 1976) and *In Re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). Applicants maintain that the Examiner has not presented a preponderance of evidence why applicants' disclosure is not adequate to satisfy the written description requirement.

According to M.P.E.P. §2163(I), "[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cas, Inc. v. Mahurkar*, 935 F2d. [1555] at 1563, 19 USPQ2d [1111] at 1116 [(Fed. Cir. 1991)]."

M.P.E.P. §2163(I) further states that "[a]n applicant shows possession of the claimed invention by describing the claimed invention with all its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F3d. 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction of practice, or by showing that the invention was 'ready for patenting' such as the disclosure of drawings or structural formulas that show that the invention was complete, or by describing distinguishing characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g. *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S. Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly* [supra], 119 F3d. at 1568, 43 USPQ2d at 1406; *Amgen Inc. v. Chugai Pharmaceutical*, 927 F2d. 1200, 1206, 18 USPQ2d 016,

1021 (Fed. Cir. 1991) (one must define a compound by 'whatever characteristics sufficiently distinguish it'). 'Compliance with the written description requirement is essentially a fact-based inquiry that 'necessarily var[ies] depending on the nature of the invention claimed'' *Enzo Biochem* [*Inc., v. Gen-Probe Inc.*], 323 F3d. [956] at 963, 63 USPQ2d [1609] at 1613 [(Fed. Cir. 2002)]." (emphasis added).

Applicants maintain that according to M.P.E.P. §2163(II)(A)(3)(a), characteristics which provide evidence that applicant was in possession of the claimed invention are: "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between structure and function, or some combination of such characteristics." (See *Enzo Biochem* [supra], 323 F.3d at 964, 63 USPQ2d at 1613). Furthermore, M.P.E.P. §2163(II)(A)(3)(a) indicates that for biomolecules, "examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length." (emphasis added)

As explained by the Court of Appeals for the Federal Circuit in *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001 [(Fed. Cir. 2006)], "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." (emphasis added).

Applicants note that as indicated in M.P.E.P. §2163(II)(A)(3)(a)(1), "there is an inverse correlation between the level of skill in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)." (emphasis added) In addition, M.P.E.P. §2163(II)(A)(2), citing *Vas-Cath* [supra], indicates that "if

a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the written description requirement is met."

With regard to the Examiner's first rationale, applicants maintain that the Court of Appeals for the Federal Circuit specifically addressed the question of adequate written description in the context of a claimed antibody in *Noelle v. Lederman*, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (2004). In *Noelle*, the Court stated that disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its affinity to that antigen. Applicants maintain that the invention as recited in amended claim 51, i.e. an isolated antibody *which binds to a human CCR5 chemokine receptor on the surface of a CD4+ cell*, is an antibody claimed by its affinity to an antigen. Applicants note that, as the Examiner acknowledged on page 4 of the June 15, 2006 Final Office Action, the human CCR5 chemokine receptor sequence was in the public domain. Applicants further note that page 33, lines 3-17 and page 34, lines 23-30 of the specification describe the expression of the human CCR5 receptor in a CD4+ cell. Accordingly, applicants maintain that the specification provides an adequate written description for the claimed antibody defined by its affinity to a well known and fully characterized antigen, i.e. the human CCR5 chemokine receptor on the surface of a CD4+ cell.

Furthermore, applicants maintain that sufficient identifying characteristics of the claimed antibody are recited in amended claim 51 and described in the specification, i.e. an antibody *which binds to the human CCR5 chemokine receptor on the surface of a cell* and *inhibits fusion of HIV-1 or a HIV-1 infected cell to a CD4+ cell*. In this regard, the specification discloses, *inter alia*, at page 22, lines 8-30, CD4+ mammalian cells incapable of fusing with Hela-env_{JR-FL} or Hela-env_{LAI} cells prior to expressing the human CCR5 chemokine receptor on their surface. Such CD4+ cells after the human CCR5

chemokine receptor is expressed on their surface are able to fuse to Hela-env_{JR-FL} or Hela-env_{LAI} cells. The specification also discloses at page 31, lines 6-11 and in Table 3, that expression of the human CCR5 chemokine receptor in Hela-CD4+ cells rendered these cells readily infectible by primary HIV-1 strains in the env-complementation assay of HIV-1 entry, thus establishing that CCR5 is necessary for HIV-1 infection of these CD4+ cell.

Response to Examiner's Rationale #2

In response to the Examiner's rationale 2, applicants maintain that the specification adequately describes the claimed genus of antibodies to CCR5. Specifically, the specification discloses how to obtain the sequence of CCR5, which was already known in the art as of the effective filing date of the subject application. The specification also discloses how to make the claimed antibodies by expressing on the surface of a CD4+ cell the human CCR5 chemokine receptor protein encoded by the CCR5 nucleic acid sequence and then using these resulting transfected cells to generate antibodies by routine methods well known in the art. In addition, as stated above, the specification discloses that the claimed antibody inhibits the fusion of HIV-1 to CD4+/CCR5+ cells.

According to M.P.E.P. §2163(II)(A)(3)(a)(1)(ii), "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see [2163(II)(A)(3)(a)(1)]i)(A), above), reduction to drawings (see [2163(II)(A)(3)(a)(1)]i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see [2163(II)(A)(3)(a)(1)]i)(C), above). See *Eli Lilly* [supra], 119 F.3d at 1568, 43 USPQ2d at 1406." Furthermore, M.P.E.P. §2163(II)(A)(3)(a)(1)(ii) states that "[w]hat constitutes a

'representative number' is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a 'representative number' depends on whether one skilled in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed."

Applicants maintain that the skill and knowledge in the relevant art was high as of the effective filing date of the application. Thus, raising antibodies against a known antigen was routine. Applicants also maintain that the identifying characteristics and common attributes of the genus of claimed antibodies in amended claim 51 is adequately disclosed in the specification. Specifically, the common features of the claimed genus are (1) binding to the human CCR5 chemokine receptor on the surface of a CD4+ cell, and (2) inhibiting fusion of HIV-1, or a HIV-1-infected cell, to such a CD4+ cell. Indeed, the specification discloses, *inter alia* at page 28, line 23 to page 29, line 7 and Table 2, that the claimed antibodies have an inhibitory effect on fusion between CD4+/CCR5+ cells, e.g. PM1 cells, and Hela-env_{JR-FL} but have no inhibitory effect between such cells and Hela-env_{LAI}, thus confirming the specificity of the fusion process. Accordingly, applicants maintain that the disclosed identifying characteristics and common features of the claimed antibodies, coupled with the high level of skill in the art as of the effective filing date of the subject application, provide an adequate written description for the claimed genus.

For the foregoing reasons, applicants maintain that the specification when combined with the knowledge in the art readily convey to one skilled in the art that applicants were in possession of the claimed invention as of the effective filing date of their application. Accordingly, applicants maintain that the specification satisfies the written description requirement of 35 U.S.C. §112, first paragraph, with regard to amended claim 51 and claims 53-60 dependent thereon, and request that the Excaminer reconsider and withdraw this ground of rejection.

Obviousness-Type Double Patenting Rejections

1. Over Claims 98, 100-104 and 118-134 of U.S. Serial No. 09/594,983

The Examiner provisionally rejected previously pending claims 51 and 53-58 as allegedly unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 98, 100-104 and 118-134 of U.S. Serial No. 09/594,983. The Examiner alleged that although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a same product.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Without conceding the correctness of the Examiner's position, applicants note that this is a provisional rejection over the U.S. Serial No. 09/594,983 which is not an allowed application. Accordingly, if the claims of the subject application are otherwise allowable, the provisional double patenting rejection should be withdrawn and the claims in the subject application should be allowed to issue, whereupon the claims of the U.S. Serial No. 09/594,983 could be assessed in terms of whether an obviousness-type double patenting rejection over a patent issued from the subject application would be warranted.

2. Over Claims 99-108 of U.S. Serial No. 10/763,545

The Examiner provisionally rejected previously pending claims 51 and 56-58 as allegedly unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 99-108 of U.S. Serial No. 10/763,545. The Examiner alleged that although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a same product.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Without conceding the correctness of the

Examiner's position, applicants note that this is a provisional rejection over the U.S. Serial No. 10/763,545 which is not an allowed application. Accordingly, if the claims of the subject application are otherwise allowable, the provisional double patenting rejection should be withdrawn and the claims in the subject application should be allowed to issue, whereupon the claims of the U.S. Serial No. 10/763,545 could be assessed in terms of whether an obviousness-type double patenting rejection over a patent issued from the subject application would be warranted.

3. Over Claims 1-5, 18 and 31 of U.S. Serial No. 10/371,483

The Examiner maintained the provisional rejection of previously pending claims 51 and 53-58 as allegedly unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 1-5, 18 and 31 of U.S. Serial No. 10/371,483.

In response, applicants respectfully traverse this obviousness-type double patenting rejection. Without conceding the correctness of the Examiner's position, applicants note that U.S. Serial No. 10/371,483 is now U.S. Patent No. 7,122,185 issued October 17, 2006. Applicants maintain that if upon entry of this Amendment, the pending claims are otherwise deemed allowable, applicants will consider filing a Terminal Disclaimer.

In view of the remarks set forth above, applicants respectfully request that the Examiner reconsider and withdraw the grounds of rejection set forth in the June 15, 2006 Final Office Action, and respectfully request allowance of claim 51, as amended, and claims 53-60 dependent thereon.

Supplemental Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the PTO-1449 (substitute) form attached hereto as **Exhibit A.**

In accordance with 37 C.F.R. §1.92(a)(2)(ii), copies of U.S. Patents and U.S. Patent Application Publications need not be provided. Accordingly, copies of documents listed below as items 1-32 are not submitted herewith. Copies of the documents listed below as items 33-232 are attached hereto as **Exhibits 1-200.**

1. U.S. Patent No. 6,258,527 issued July 10, 2001 to D. Littman et al.;

2. U.S. Patent No. 6,258,782 issued July 10, 2001 to S. Barney et al;

3. U.S. Patent No. 6,692,745 issued February 17, 2004 to W.C. Olson et al.;

4. U.S. Patent No. 6,972,126 issued December 6, 2005 to G.P. Allaway et al.;

5. U.S. Patent No. 5,939,320 issued August 17, 1999 to D. Littman et al.;

6. U.S. Patent No. 5,126,433 issued December 21, 1989 to P.J. Maddon et al.;

7. U.S. Patent No. 5,071,964 issued December 10, 1991 to M. Dustin et al.;

8. U.S. Patent No. 5,091,513 issued February 25, 1992 to J. Huston et al.;

9. U.S. Patent No. 5,215,913 issued June 1, 1993 to M.R. Posner et al.;

10. U.S. Patent No. 5,225,539 issued July 6, 1993 to G.P. Winter et al.;

11. U.S. Patent No. 5,603,933 issued February 18, 1997 to V.A. Dwyer et al.;

12. U.S. Patent No. 5,668,149 issued September 16, 1997 to S. Oroszlan et al.;

13. U.S. Patent No. 5,817,767 issued October 6, 1998 to G.P. Allaway et al.;

14. U.S. Patent No. 5,854,400 issued December 29, 1998 to T. Chang et al.;

15. U.S. Patent No. 4,886,743 issued December 12, 1989 to L.E. Hood et al.;

16. U.S. Patent No. 6,100,087 issued August 8, 2000 to J. Rossi et el.;

17. U.S. Patent No. 6,261,763 B1 issued July 17, 2001 to G.P. Allaway et al.;

18. U.S. Patent No. 6,930,174 issued August 16, 2005 to M. Samson et al.;

19. U.S. Patent No. 7,118,859 issued October 10, 2006 to V.M. Litwin et al.;

20. Y. Li et al., U.S. Patent Application Publication No. 2003-0023044 published January 30, 2003;

21. P.W. Gray et al., U.S. Patent Application Publication No. 2005-0260565 published November 24, 2005;

22. L. Wu et al., U.S. Patent Application Publication No. 2003-0166870 published December 23, 2004,

23. C. Combadiere et al., U.S. Patent Application Publication No. 2004-0259785 published December 23, 2004;

24. C. Combadiere et al., U.S. Patent Application Publication No. 2003-0195348 published October 16, 2003;

25. D. Littman et al., U.S. Patent Application Publication No. 2003-0096221 published May 22, 2003;

26. L. Lopalco et al., U.S. Patent Application Publication No. 2003-0003440 published January 2, 2003;

27. G.P. Allaway et al., U.S. Patent Application Publication No. 2006-0029932 published February 09, 2006;

28. G.P. Allaway et al., U.S. Patent Application Publication No. 2006-0140977 published June 29, 2006;

29. G.P. Allaway et al., U.S. Patent Application Publication No. 2002-0045161 published April 18, 2002;

30. W.C. Olson et al., U.S. Patent Application Publication No. 2004-0062767 published April 01, 2004;

31. G.P. Allaway et al., U.S. Patent Application Publication No. 2006-0194244 published August 31, 2006;

32. G.P. Allaway et al., U.S. Patent Application Publication No. 2006-0233798 published October 19, 2006;

33. Pending claims in W.C. Olson et al., U.S. Patent Application Serial No. 11/581,944 filed October 16, 2006 **(Exhibit 1)**;

34. Pending claims in W.C. Olson et al., U.S. Patent Application Serial No. 11/581,945 filed October 16, 2006 **(Exhibit 2)**;

35. Pending claims in W.C. Olson et al., U.S. Patent Application Serial No. 11/520,556 filed September 12, 2006 **(Exhibit 3)**;

36. Pending claims in V.M. Litwin et al., U.S. Patent Application Serial No. 11/544,346 filed October 5, 2006 **(Exhibit 4)**;

37. Pending claims in W.C. Olson et al., U.S. Patent Application Serial No. 11/316,078 filed December 21, 2005 **(Exhibit 5)**;

38. Pending claims in G.P. Allaway et al., U.S. Patent Application Serial No. 11/258,963 filed October 25, 2005 **(Exhibit 6)**;

39. PCT International Application Publication No. WO 92/01451 published February 6, 1992 **(Exhibit 7)**;

40. PCT International Application Publication No. WO 95/16789 published June 22, 1995 **(Exhibit 8)**;

41. PCT International Application Publication No. WO 97/28258 published August 7, 1997 **(Exhibit 9)**;

42. PCT International Application Publication No. WO 98/18826 published May 7, 1998 **(Exhibit 10)**;

43. PCT International Application Publication No. WO 01/55439 A1 published August 2, 2001 **(Exhibit 11)**;

44. PCT International Application Publication No. WO 94/22477 published October 13, 1994 **(Exhibit 12)**;

45. Abaza, M.S.I et al., (1992) "Effects Of Amino Acid Substitutions Outside An Antigenic Site On Protein Binding To Monoclonal Antibodies Of Predetermined Specificity Obtained By Peptide Immunization: Demonstration With Region 94-100 (Antigenic Site 3) Of Myoglobin", *J. Prot. Chem.* 11(5):433-443 **(Exhibit 13)**;

46. Alexander, H. et al., (1992) "Altering The Antigenicity Of Proteins", *Proc. Natl. Acad. Sci.* 89:3352-3356 **(Exhibit 14)**;

47. Alkhatib et al., (1996) Abstract At 3rd Conference On Retroviruses **(Exhibit 15)**;

48. Allan, J., (1997) "Human Immunodeficiency Virus-Related Infections In Animal Model Systems", In *AIDS: Biology, Diagnosis, Treatment And Prevention,* 4th Edition, Lippincott-Raven Publishers, Philadelphia, Pp 15-27 **(Exhibit 16)**;

49. Allaway, G.P. et al., (1993) "Synergistic Inhibition Of HIV-1 Envelope-Mediated Cell Fusion By CD4-Based Molecules In Combination With Antibodies To gp120 Or gp41", *AIDS Res. Hum. Retroviruses* 9:581-587 **(Exhibit 17)**;

50. Allaway, G.P. et al., (1995) "Expression And Characterization Of CD4-IgG2, A Novel Heterotetramer That Neutralizes Primary HIV Type 1 Isolates", *AIDS Res. Hum. Retrovirus* 11:533-539 **(Exhibit 18)**;

51. Amara, A. et al., (1997) "HIV Coreceptor Downregulation As Antiviral Principle: SDF-1α-Dependent Internalization Of The Chemokine Receptor CXCR4 Contributes To Inhibition Of HIV Replication", *J. Exp. Med.* 186:139-146 **(Exhibit 19)**;

52. Arthos, J. et al., (1989) "Identification Of The Residues In Human CD4 Critical For The Binding Of HIV", *Cell* 57:469-481 **(Exhibit 20)**;

53. Ashorn, P.A. et al., (1990) "Human Immunodeficiency Virus Envelope Glycoprotein/CD4 Mediated Fusion Of Nonprimate Cells With Human Cells", *J. Virol.* 64:2149-2156 **(Exhibit 21)**;

54. Attanasio, R. et al., (1991) "Anti-Idiotypic Antibody Response To Monoclonal Anti-CD4 Preparations In Nonhuman Primate Species", *J. Immunol.* 146:507-514 **(Exhibit 22)**;

55. Baba, M. et al., (1988) "Mechanism Of Inhibitory Effect Of Dectran Sulfate And Heparin On Replication Of Human Immunodeficiency Virus *In Vitro*", *Proc. Natl. Acad. Sci.* 85:6132-6136 **(Exhibit 23)**;

56. Back, D.J., (1999) "Pharmacological Issues Relating To Viral Resistance", *Infection* 27 (Suppl. 2):S42-S44 **(Exhibit 24)**;

57. Baulerle, P.A. and Huttner, W.B., (1987) "Tyrosine Sulfation Is A Trans-Golgi-Specific Protein Modification", *Cell. Biol.* 105:2655-2664 **(Exhibit 25)**;

58. Benet et al. (1990) "Pharmacokinetics: The Dynamics Of Drug Absorption, Distribution And Elimination" In *Goodman And Gilman's The Pharmacological Basis Of Therapeutics,* Gilman Et El., Eds. Pergamon Press, New York, Pp 3-32 **(Exhibit 26)**;

59. Berger, E.A. et al (1996) Abstract No. 002, 8 At Keystone Symposium **(Exhibit 27)**;

60. Berger, E.A., (1997) "HIV Entry And Tropism: The Chemokine Receptor Connection", *AIDS* 11(Suppl A):S3-S16 **(Exhibit 28)**;

61. Bieniasz, P.D. et al., (1997) "HIV-1 Induced Cell Fusion Is Mediated By Multiple Regions Within Both The Viral Envelope And The CCR5 Co-Receptor", *EMBO* 16:2599-2609 **(Exhibit 29)**;

62. Blanpain, C. et al., (1999) "Multiple Charged And Aromatic Residues In CCR5 Amino-Terminal Domain Are Involved In High Affinity Binding Of Both Chemokines And HIV-1 Env Protein", *J. Biol. Chem.* 274:34719-34727 **(Exhibit 30)**;

63. Brelot, A. et al., (1997) "Role Of The First And Third Extracellular Domains Of CXCR4 In Human Immunodeficiency Virus Coreceptor Activity", *J. Virol.* 71:4744-4751 **(Exhibit 31)**;

64. Broder, C.C. et al., (1993) "The Block To HIV-1 Envelope Glycoprotein-Mediated Membrane Fusion In Animal Cells Expressing Human CD4 Can Be Overcome By A Human Cell Component(s)", *Virol.* 193:483-491 **(Exhibit 32)**;

65. Broder, C.C. et al., (1996) "HIV And The 7-Transmembrane Domain Receptors", *Pathobiology* 64(4):171-179 **(Exhibit 33)**;

66. Burkly, L. et al., (1995) "Synergistic Inhibition Of Human Immunodeficiency Virus Type 1 Envelope Glycoprotein-Mediated Cell Fusion And Infection By An Antibody To CD4 Domain 2 In Combination With Anti-gp-120 Antibodies", *J. Virol.* 69:4267-4273 **(Exhibit 34)**;

67. Burton, D.R. et al., (1994) "Efficient Neutralization Of Primary Isolates Of HIV-1 By A Recombinant Human Monoclonal Antibody", *Science* 266:1024-1027 **(Exhibit 35)**;

68. Busso, M. et al., (1991) "HIV-Induced Syncytium Formation Requires The Formation Of Conjugates Between Virus-Infected And Uninfected T-Cells In Vitro", *AIDS* 5:1425-1432 **(Exhibit 36)**;

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70. Capon, D.J. et al., (1989) "Designing CD4 Immunoadhesions For AIDS Therapy", *Nature* 337:525-531 **(Exhibit 38)**;

71. Chams, V. et al., (1992) "Simple Assay To Screen For Inhibitors Of Interaction Between The Human Immunodeficiency Virus Envelope

Glycoprotein And Its Cellular Receptor, CD4", *Antimicrob Agents Chemother.* 36(2):262-272 **(Exhibit 39)**;

72. Chan, D.C. et al., (1998) "Evidence That A Prominent Cavity In The Coiled Coil Of HIV Type 1 gp41 Is An Attractive Drug Target", *Proc. Natl. Acad. Sci.* 95:15613-15617 **(Exhibit 40)**;

73. Chan, D.C. et al., (1998) "HIV Entry And Its Inhibition", *Cell* 93:681-684 **(Exhibit 41)**;

74. Charo, I.F. et al., (1994) "Molecular Cloning And Functional Expression Of Two Monocyte Chemoattractant Protein 1 Receptors Reveals Alternative Splicing Of The Carboxyl-Terminal Tails", *Proc. Natl. Acad. Sci.* 91:2752-2756 **(Exhibit 42)**;

75. Chen, Z. et al., (1997) "Genetically Divergent Strains Of Simian Immunodeficiency Virus Use CCR5 As A Coreceptor For Entry", *J. Virol.* 71(4):2705-2714 **(Exhibit 43)**;

76. Clapham, P.R. et al., (1989) "Soluble CD4 Blocks The Infectivity Of Diverse Strains Of HIV And SIV For T Cells And Monocytes But Not For Brain And Muscle Cells", *Nature* 337:368-370 **(Exhibit 44)**;

77. Clapham, P.R. et al., (1991) "Specific Cell Surface Requirements For The Infection Of CD4-Positive Cells By Human Immunodeficiency Virus Types 1 And 2 By Simian Immunodeficiency Virus", *Virol.* 181:703-715 **(Exhibit 45)**;

78. Co. M.S. et al., (1991) "Humanized Antibodies For Antiviral Therapy", *Proc. Natl. Acad. Sci.* 88:2869-2873 **(Exhibit 46)**;

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80. Combadiere, C. et al., (1996) "Cloning And Functional Expression Of CC CKR5, A Human Monocyte CC Chemokine Receptor Selective For MIP-1α, MIP-1β And RANTES", *J. Leukoc. Biol.* 60:147-152 **(Exhibit 48)**;

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232. Supplementary Partial European Search Report Issued February 19, 2003 for European Patent Application No. 98931261 **(Exhibit 200).**

U.S. Patent Application Serial No. 11/581,944 (item 33) filed October 16, 2006 is a continuation of U.S. Patent Application Serial No. 10/371,483 filed February 21, 2003, now U.S. Patent Number 7,122,185. In accordance with 37 C.F.R. §1.98(c), a copy of item 33 need not be submitted because its disclosure is substantively cumulative to that of U.S. Patent Number 7,122,185; a copy of which has been submitted with a prior Information Disclosure Statement. However, in accordance

with 37 C.F.R. §1.98(a)(iii), a copy of the claims currently pending in U.S. Serial No. 11/581,944 is attached hereto as Exhibit 1.
U.S. Patent Application Serial No. 11/581,945 (item 34) filed October 16, 2006 is a continuation of U.S. Patent Application Serial No. 10/371,483 filed February 21, 2003, now U.S. Patent Number 7,122,185. In accordance with 37 C.F.R. §1.98(c), a copy of item 34 need not be submitted because its disclosure is substantively cumulative to that of U.S. Patent Number 7,122,185; a copy of which has been submitted with a prior Information Disclosure Statement. However, in accordance with 37 C.F.R. §1.98(a)(iii), a copy of the claims currently pending in U.S. Serial No. 11/581,945 is attached hereto as Exhibit 2.

U.S. Patent Application Serial No. 11/520,556 (item 35) filed September 12, 2006 is a continuation of U.S. Patent Application Serial No. 09/912,824 filed July 25, 2001, now U.S. Patent Number 7,138,119. In accordance with 37 C.F.R. §1.98(c), a copy of item 35 need not be submitted because its disclosure is substantively cumulative to that of U.S. Patent Number 7,138,119; a copy of which has been submitted with a prior Information Disclosure Statement. However, in accordance with 37 C.F.R. §1.98(a)(iii), a copy of the claims currently pending in U.S. Serial No. 11/520,556 is attached hereto as Exhibit 3.

U.S. Patent Application Serial No. 11/544,346 (item 36) filed October 5, 2006 is a continuation of U.S. Patent Application Serial No. 09/891,062 filed June 25, 2001, now U.S. Patent Number 7,118,859 (item 19). In accordance with 37 C.F.R. §1.98(c), a copy of item 36 need not be submitted because its disclosure is substantively cumulative to that of item 19. However, in accordance with 37 C.F.R. §1.98(a)(iii), a copy of the claims currently pending in U.S. Serial No. 11/544,346 is attached hereto as Exhibit 4.

U.S. Patent Application Serial No. 11/316,078 (item 37) filed December 21, 2005 is a continuation of U.S. Patent Application Serial No. 10/116,797 filed April 5, 2002, now U.S. Patent Number 7,060,273. In accordance with 37 C.F.R. §1.98(c), a copy of item 37 need not be submitted because its disclosure is substantively cumulative to that

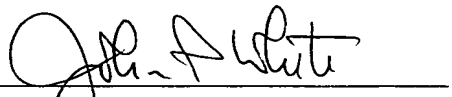
of U.S. Patent Number 7,060,273; a copy of which has been submitted with a prior Information Disclosure Statement. However, in accordance with 37 C.F.R. §1.98(a)(iii), a copy of the claims currently pending in U.S. Serial No. 11/316,078 is attached hereto as Exhibit 5.

U.S. Patent Application Serial No. 11/258,963 (item 38) filed October 25, 2005 is a continuation of U.S. Patent Application Serial No. 09/412,284 filed October 5, 1999, now U.S. Patent Number 6,972,126 (item 4). In accordance with 37 C.F.R. §1.98(c), a copy of item 38 need not be submitted because its disclosure is substantively cumulative to that of item 4. However, in accordance with 37 C.F.R. §1.98(a)(iii), a copy of the claims currently pending in U.S. Serial No. 11/581,944 is attached hereto as Exhibit 6.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the $395.00 fee for filing an RCE and the $60.00 fee for a one-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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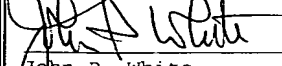

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